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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
ROMEO, DAVID S	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 03/30/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/063,672	EATON ET AL.	
	Examiner	Art Unit	
	David S. Romeo	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 December 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,9,11-14 and 17-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,9,11-14 and 17-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1204*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed 12/10/2004 has been entered. Claims 1-7, 9, 11-14, 17-20 are pending and being examined.

Inventorship

In view of the papers filed 12/10/2004, the inventorship in this nonprovisional application has been changed by the deletion of Dan L. Eaton, Ellen Filvaroff, Mary E. Gerritsen, and Colin K. Watanabe.

The application will be forwarded to the Office of Initial Patent Examination (OIPE) for issuance of a corrected filing receipt, and correction of Office records to reflect the inventorship as corrected.

Maintained Formal Matters, Objections, and/or Rejections:

Claim Rejections - 35 USC § 112

Claims 1-7, 9, 14, 17-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO: 9, does not reasonably provide enablement for nucleic acid molecules having a recited % identity to the genus of all nucleic acid molecules encoding the amino acid sequence of SEQ ID NO: 10, for the genus of all nucleic acid molecules encoding the amino acid sequence of SEQ ID NO: 10, for nucleic acid molecules having a recited % identity to SEQ ID NO: 9 without regard to the functional activity such nucleic acid molecules, or for nucleic acid molecules that hybridize to SEQ ID NO: 9 without regard to the functional activity of such

nucleic acid molecules. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Applicants argue that they have established in example 18 that the gene encoding the PRO874 polypeptide is differentially expressed in certain cancers, which indicates that the disclosed gene, degenerate and variant nucleic acid molecules which encode the SEQ ID NO: 10, and the corresponding polypeptide and antibodies thereto are useful as diagnostic tools, as indicated by the Grimaldi declaration (Exhibit 1). Applicants argue that no additional research is required to use the full scope of the claimed invention. Applicant's arguments have been fully considered but they are not persuasive. The declaration of J. Christopher Grimaldi under 37 CFR 1.132 filed 12/10/2004 (Exhibit 1) is insufficient to overcome the rejection of claims 1-7, 9, 14, 17-20 based upon a lack of enablement as set forth in the last Office action because: Declarant argues that it was determined whether the polynucleotides tested were more highly expressed, less expressed, or whether expression remained the same and that the results of these gene expression studies can be used to differentiate tumor from normal. Declarant argues that if a difference is detected, this indicates that the gene and its corresponding polypeptide and antibodies against the polypeptide are useful for diagnostic purposes. Declarant's arguments have been fully considered but they are not persuasive.

Although the specification discloses that DNA40621-1440 (SEQ ID NO: 9) is more highly expressed in normal lung than as compared to lung tumor (Example 18, Page 141), the specification provides no information regarding the level of expression, activity, or role in cancer of the PRO874 polypeptide. Further, differential tissue nucleic acid expression is not always

correlated with protein levels. For example, Allman (U) discloses that germinal center B cells express dramatically more BCL-6 protein than resting B cells, despite similar BCL-6 mRNA levels in the two cell populations. Page 5257, paragraph bridging left and right columns. mRNA translation is regulated in many genes and can be mediated by binding of proteins to cis-acting RNA motifs in the untranslated regions of the mRNAs (paragraph bridging pages 5266-5267). Furthermore, all polynucleotides and their corresponding polypeptides from a particular tumor sample can invariably be classified as either more highly expressed, less expressed, not expressed, or expression unchanged as compared to some standard level of expression. It can then be asserted that any polynucleotide and its corresponding polypeptide that is expressed in this manner can be used to detect or characterize the tumor. However, the present specification does not provide any information regarding the level of expression, activity, or role in cancer of the PRO874 polypeptide. The examiner has cited countervailing evidence to show that the skilled artisan would have a legitimate basis to question the relative expression of the PRO874 polypeptide in tumors. The skilled artisan would not know if PRO874 polypeptide expression could, would or should be upregulated, down-regulated, or unchanged in cancer. It is this additional characterization of the PRO874 polypeptide and validation of its association with lung tumors that is required in order to enable the claimed SEQ ID NO: 9 variants, degenerate and degenerate variant polynucleotides encoding SEQ ID NO: 10 and SEQ ID NO: 10 variants, respectively, that constitutes undue experimentation. The present rejection is based upon Applicants' failure to disclose to disclose enough information about the invention to make its usefulness immediately apparent to those familiar with the technological field of the invention. Accordingly, the expression of SEQ ID NO: 9 in normal lung as compared to lung tumor does

not enable the claimed SEQ ID NO: 9 variants, degenerate and degenerate variant polynucleotides encoding SEQ ID NO: 10 and SEQ ID NO: 10 variants, respectively, the only obvious use of which is in the production of SEQ ID NO: 10 and SEQ ID NO: 10 variants.

Applicants argue that they have established that the accepted understanding in the art that there is a reasonable correlation between gene expression and expression of the encoded protein, that the standard for establishing a use or utility for a claimed invention is not absolute certainty, that that a necessary correlation between mRNA and protein is not required, that it is well established in the art that protein levels are positively correlated with mRNA levels, that Allman supports Applicants' position, that the one contrary example of Allman does establish that the skilled artisan would find it more likely than not that there is no correlation between mRNA and protein levels, and that Applicants' assertions are supported by the declarations of Grimaldi (Exhibit 2) and Polakis (Exhibit 3), and the teachings in the Molecular Biology of the Cell (Exhibit 4). Applicant's arguments have been fully considered but they are not persuasive. The present rejection is based on the fact that Allman demonstrates that mRNA and protein levels do not always correlate, and that in the absence of any information regarding the level of expression, activity, or role in cancer of the PRO874 polypeptide, the skilled artisan would not know if PRO874 polypeptide expression could, would or should be upregulated, down-regulated, or unchanged in cancer, and the skilled artisan would have a legitimate basis to doubt Applicants' assertions regarding use of the PRO874 polypeptide for cancer diagnosis and treatment.

The declaration of J. Christopher Grimaldi under 37 CFR 1.132 filed 12/10/2004 (Exhibit 2) is insufficient to overcome the rejection of claims 1-7, 9, 14, 17-20 based upon a lack

of enablement as set forth in the last Office action because: Declarant argues that comparison of gene expression levels in normal versus diseased tissue has important implications, that two cell samples that have differing mRNA concentrations for a specific gene are expected to have correspondingly different concentrations of protein for that gene, that if the dogma that a change in mRNA will represent a similar change in protein did not hold true then techniques used to detect mRNA would have little value and not be so widely used, and that the detection of increased or decreased polypeptide expression can be used for cancer diagnosis and treatment. Declarant's arguments have been fully considered but they are not persuasive. All polynucleotides and their corresponding polypeptides from a particular tumor sample can invariably be classified as either more highly expressed, less expressed, not expressed, or expression unchanged as compared to some standard level of expression. It can then be asserted that any polynucleotide and its corresponding polypeptide that is expressed in this manner can be used to detect or characterize the tumor. However, the present specification does not provide any information regarding the level of expression, activity, or role in cancer of the PRO874 polypeptide. The examiner has cited countervailing evidence to show that the skilled artisan would have a legitimate basis to question the relative expression of the PRO874 polypeptide in tumors. The skilled artisan would not know if PRO874 polypeptide expression could, would or should be upregulated, down-regulated, or unchanged in cancer. It is this additional characterization of the PRO874 polypeptide and validation of its association with lung tumors that is required in order to enable the claimed SEQ ID NO: 9 variants, degenerate and degenerate variant polynucleotides encoding SEQ ID NO: 10 and SEQ ID NO: 10 variants, respectively, that constitutes undue experimentation. The present rejection is based upon Applicants' failure

to disclose to disclose enough information about the invention to make its usefulness immediately apparent to those familiar with the technological field of the invention. Accordingly, the expression of SEQ ID NO: 9 in normal lung as compared to lung tumor does not enable the claimed SEQ ID NO: 9 variants, degenerate and degenerate variant polynucleotides encoding SEQ ID NO: 10 and SEQ ID NO: 10 variants, respectively, the only obvious use of which is in the production of SEQ ID NO: 10 and SEQ ID NO: 10 variants.

Declarant argues that even in cases where protein and mRNA expression do not correlate, this still provides significant information useful for cancer diagnosis and treatment because it enables more accurate tumor classification and hence better determination of a suitable therapy. Declarant's arguments have been fully considered but they are not persuasive. In effect, Declarant's position is that the claimed polynucleotides encoding the PRO874 polypeptide are enabled because those of skill in the art could experiment with them and figure out for themselves what any observed experimental results might mean. The examiner does not agree that such a disclosure enables the claimed SEQ ID NO: 9 variants, degenerate and degenerate variant polynucleotides encoding SEQ ID NO: 10 and SEQ ID NO: 10 variants, respectively. This further characterization is part of the act of invention and until it has been undertaken, Applicants' invention is incomplete. Thus, a considerable inventive effort is required on the part of the skilled practitioner in order to practice the full scope of the claimed invention.

The declaration of Paul Polakis under 37 CFR 1.132 filed 12/10/2004 is insufficient to overcome the rejection of claims 1-7, 9, 14, 17-20 based upon a lack of enablement as set forth in the last Office action because: Declarant states that the primary focus of the Tumor Antigen Project was to identify tumor cell markers useful as targets for cancer diagnostics and

therapeutics. Dr. Polakis states that approximately 200 gene transcripts were identified that are present in human tumor cells at significantly higher levels than in corresponding normal human cells. Declarant states that antibodies to approximately 30 of the tumor antigen proteins have been developed and used to show that approximately 80% of the samples show correlation between increased mRNA levels and changes in protein levels. Declarant states that an increased level of mRNA in a tumor cell relative to normal cell typically correlates to a similar increase in the encoded protein. Declarant states that it remains a central dogma in molecular biology that increased mRNA levels are predictive of corresponding increased levels of the encoded protein. Dr. Polakis characterizes the reports of instances where such a correlation does not exist as exceptions to the rule. Declarant's arguments have been fully considered but they are not persuasive. The present application provides no information regarding the level of expression, activity, or role in cancer of the PRO874 polypeptide. Only mRNA expression data was presented. The present rejection is based upon Applicants' failure to disclose to disclose enough information about the invention to make its usefulness immediately apparent to those familiar with the technological field of the invention. The examiner has cited countervailing evidence to show that the skilled artisan would have a legitimate basis to question the relative expression of the PRO874 polypeptide in tumors. The skilled artisan would not know if PRO874 polypeptide expression could, would or should be upregulated, down-regulated, or unchanged in cancer. It is this additional characterization of the PRO874 polypeptide and validation of its association with lung tumors that is required in order to enable the claimed SEQ ID NO: 9 variants, degenerate and degenerate variant polynucleotides encoding SEQ ID NO: 10 and SEQ ID NO: 10 variants, respectively, that constitutes undue experimentation. Accordingly, the

expression of SEQ ID NO: 9 in normal lung as compared to lung tumor does not enable the claimed SEQ ID NO: 9 variants, degenerate and degenerate variant polynucleotides encoding SEQ ID NO: 10 and SEQ ID NO: 10 variants, respectively, the only obvious use of which is in the production of SEQ ID NO: 10 and SEQ ID NO: 10 variants. Furthermore, a "dogma" is an authoritative principle, belief, or statement of ideas or opinion, especially one considered to be absolutely true. Allman provides evidence that Polakis's asserted dogma is not absolutely true and that the skilled artisan would have a legitimate basis to doubt the utility of the PRO874 polypeptide based solely on the disclosure regarding DNA40621-1440 in Example 18 on page 141 of the present specification.

The teachings in the Molecular Biology of the Cell (Exhibit 4) are acknowledged. However, in the present case the specification does not provide any testing of the level of expression, activity, or role in cancer of the PRO874 polypeptide. The skilled artisan would not know if PRO874 polypeptide expression could, would or should be upregulated, down-regulated, or unchanged in cancer.

Applicants argue that the claimed polynucleotides would be enabled for use as a diagnostic tool even if there is no direct correlation between gene expression and protein expression because the identification of both gene expression and protein expression enables more accurate tumor classification and better determination of therapy, as evidenced by the paragraph 6 of the Grimaldi declaration (Exhibit 2), as echoed by the Ashkenazi declaration (Exhibit 5), and as further supported by Hanna (Exhibit 6).

Applicant's arguments have been fully considered but they are not persuasive.

Paragraph 6 of the declaration of J. Christopher Grimaldi under 37 CFR 1.132 filed 12/10/2004 (Exhibit 2) is insufficient to overcome the rejection of claims 1-7, 9, 14, 17-20 based upon a lack of enablement as set forth in the last Office action because: Declarant argues that even in cases where protein and mRNA expression do not correlate, this still provides significant information useful for cancer diagnosis and treatment because it enables more accurate tumor classification and hence better determination of a suitable therapy. Declarant's arguments have been fully considered but they are not persuasive. In effect, Declarant's position is that the claimed polynucleotides and the encoded polypeptides are useful because those of skill in the art could experiment with them and figure out for themselves what any observed experimental results might mean. The examiner does not agree that such a disclosure enables the claimed SEQ ID NO: 9 variants, degenerate and degenerate variant polynucleotides encoding SEQ ID NO: 10 and SEQ ID NO: 10 variants, respectively, the only obvious use of which is in the production of SEQ ID NO: 10 and SEQ ID NO: 10 variants. This further characterization is part of the act of invention and until it has been undertaken, Applicants' invention is incomplete. Thus, a considerable inventive effort is required on the part of the skilled practitioner in order to practice the full scope of the claimed invention.

The declaration of Dr. Ashkenazi under 37 CFR 1.132 filed 12/10/2004 (Exhibit 5) is insufficient to overcome the rejection of claims 1-7, 9, 11-13 based upon a lack of scope of enablement as set forth in the last Office action because: Declarant asserts that amplification of certain genes gives cancer cells an advantage relative to normal cells. Declarant asserts that if the mRNA and gene product are over-expressed, then the gene product is a promising candidate for therapy. Declarant's arguments have been fully considered but they are not persuasive. The

present claims are directed to or encompass SEQ ID NO: 9 variants, degenerate and degenerate variant polynucleotides encoding SEQ ID NO: 10 and SEQ ID NO: 10 variants, respectively, the only obvious use of which is in the production of SEQ ID NO: 10 and SEQ ID NO: 10 variants. The present specification discloses:

> The PRO polypeptides and nucleic acid molecules of the present invention may also be used diagnostically for tissue typing, wherein the PRO polypeptides of the present invention may be differentially expressed in one tissue a: compared to another, preferably in a diseased tissue as compared to a normal tissue of the same tissue type. PRO nucleic acid molecules will find use for generating probes for PCR, Northern analysis, Southern analysis and Western analysis. Page 93, paragraph 0336.
>
> Identification of the differential expression of the PRO polypeptide-encoding nucleic acid in one or more tumor tissues as compared to one or more normal tissues of the same tissue type renders the molecule useful diagnostically for the determination of the presence or absence of tumor in a subject suspected of possessing a tumor as well as therapeutically as a target for the treatment of a tumor in a subject possessing such a tumor. Page 140, paragraph 0530.
>
> DNA40621-1440 is more highly expressed in normal lung than as compared to lung tumor. Example 18, Page 141.

However, no information is provided in the differential expression of the PRO polypeptide-encoding nucleic acid data regarding the level of expression, activity, or role in cancer of the PRO874 polypeptide. Declarant asserts that a gene protein product of an amplified gene is useful regardless of the expression level of the protein because parallel monitoring of gene amplification and protein expression provides better tumor diagnosis, treatment, or classification. Declarant's arguments have been fully considered but they are not persuasive. As discussed above, no information is provided in the differential expression of the PRO polypeptide-encoding nucleic acid data regarding the level of expression, activity, or role in cancer of the PRO874 polypeptide. The specification fails to disclose enough information about

the invention to make its usefulness immediately apparent to those familiar with the technological field of the invention. The examiner accepts for argument's sake that a person skilled in the art could derive some data regarding PRO874 polypeptide expression in tumors in which PRO874 mRNA is differentially expressed. The examiner can also accept, for argument's sake, that such data could be used to correlate PRO874 polypeptide expression with PRO874 polynucleotide amplification or PRO874 mRNA differential expression. The skilled artisan might also be able to derive a practical way of using this data. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicants' invention is incomplete. In effect, Declarant's position is that the claimed polynucleotides and the encoded polypeptides are useful because those of skill in the art could experiment with them and figure out for themselves what any observed experimental results might mean. The examiner does not agree that such a disclosure enables the claimed SEQ ID NO: 9 variants, degenerate and degenerate variant polynucleotides encoding SEQ ID NO: 10 and SEQ ID NO: 10 variants, respectively, the only obvious use of which is in the production of SEQ ID NO: 10 and SEQ ID NO: 10 variants. This further characterization is part of the act of invention and until it has been undertaken, Applicants' invention is incomplete. Thus, a considerable inventive effort is required on the part of the skilled practitioner in order to practice the full scope of the claimed invention.

It is acknowledged that, in general, FISH and HIC results with HER-2/neu correlate well (Hanna, Exhibit 6). However, discordant results are seen and the significance of these results is unclear (Hanna, first page, right column, last paragraph). Hanna states that HER-2/neu testing will utilize IHC as a screen, followed by FISH in IHC-negative cases (first page, right column,

last paragraph), presumably to better understand the significance of these discordant results. This teaching does not provide a specific benefit in currently available form for the presently claimed polynucleotides. Therefore, in view of the evidence that protein levels are not always consistent with protein levels, Hanna supports the examiner's position that the differential expression data of DNA40621-1440 does not enable the claimed SEQ ID NO: 9 variants, degenerate and degenerate variant polynucleotides encoding SEQ ID NO: 10 and SEQ ID NO: 10 variants, respectively, the only obvious use of which is in the production of SEQ ID NO: 10 and SEQ ID NO: 10 variants.

Claims 1-7, 9, 14, 17-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants argue that the current invention is adequately described because the skill level is high, and that based on the cloning and expression of PRO874, the description of the gene amplification assay, the actual reduction to practice of SEQ ID NO: 9 and SEQ ID NO: 10, and the functional limitation, the skilled artisan would know that Applicants were in possession of the claimed invention. Applicant's arguments have been fully considered but they are not persuasive.

The claims have been amended to recite the limitation "wherein said isolated polypeptide is more highly expressed in normal lung tissue compared to lung tumor, or wherein said isolated

polypeptide is encoded by a polynucleotide that is more highly expressed in normal lung tissue compared to lung tumor." The present specification discloses:

> The PRO polypeptides and nucleic acid molecules of the present invention may also be used diagnostically for tissue typing, wherein the PRO polypeptides of the present invention may be differentially expressed in one tissue a: compared to another, preferably in a diseased tissue as compared to a normal tissue of the same tissue type. PRO nucleic acid molecules will find use for generating probes for PCR, Northern analysis, Southern analysis and Western analysis. Page 93, paragraph 0336.
>
> Identification of the differential expression of the PRO polypeptide-encoding nucleic acid in one or more tumor tissues as compared to one or more normal tissues of the same tissue type renders the molecule useful diagnostically for the determination of the presence or absence of tumor in a subject suspected of possessing a tumor as well as therapeutically as a target for the treatment of a tumor in a subject possessing such a tumor. Page 140, paragraph 0530.
>
> DNA40621-1440 is more highly expressed in normal lung than as compared to lung tumor. Example 18, Page 141.

The only obvious use of the claimed SEQ ID NO: 9 variants, SEQ ID NO: 9 variants, degenerate and degenerate variant polynucleotides encoding SEQ ID NO: 10 and SEQ ID NO: 10 variants, respectively, is in the production of SEQ ID NO: 10 and SEQ ID NO: 10 variants. However, the present application provides no information regarding the level of expression, activity, or role of the PRO874 polypeptide in cancer. To the extent that Applicants rely on a central dogma, a significant probability, or reasonable correlation as discussed in their reply to the last Office action for expression of the PRO 874 polypeptide, these arguments have been fully considered but they are not persuasive for the same reasons that they were not persuasive in the rejection for lack of enablement.

It is noted that claim 14 does not contain a functional limitation other than the hybridization language.

The disclosure of only one species encompassed within a genus adequately describes a claim directed to that genus only if the disclosure indicates that Applicants have invented species sufficient to constitute the genus. An Applicant for a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from species other than those specifically enumerated. An Applicant will not be deemed to have invented species sufficient to constitute the genus by virtue of having disclosed a single species when the evidence indicates ordinary artisans could not predict the operability in the invention of any species other than the one disclosed.

The present specification provides a single example of a naturally occurring nucleic acid molecule (DNA40621-1440 or SEQ ID NO: 9) that is more highly expressed in normal lung as compared to lung tumor. The specification does not provide any information regarding the occurrence of SEQ ID NO: 9 variants or degenerate polynucleotides in nature and it is unpredictable which of those sequences, if any other than the native SEQ ID NO: 9 sequence, would be a native PRO polynucleotide encoding a native PRO polypeptide or would be more highly expressed in normal lung as compared to lung tumor. No information is provided regarding the expression or activity of the encoded polypeptide (PRO874) in normal or tumor tissue. The present specification does not provide any evidence that Applicants constructed any variant polynucleotides or polypeptides or determined that any of such variant polynucleotides or polypeptides were more highly expressed in normal lung tissue compared to lung tumor.

The examiner accordingly finds that the species exemplified, identified, or otherwise described with particularity is not representative of the functional genera implied by the *minimal* structural and functional limitations imposed by the claims, and that the skilled artisan would

thus not have recognized that the inventors were in possession of the invention now claimed at the time the application was filed.

New Formal Matters, Objections, and/or Rejections:

Claim Rejections - 35 USC § 112

Claims 1-7, 9, 11-14, 17-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Support for the limitation "amino acids 34-321 of SEQ ID NO: 10" (claims 1-7, 9, 11-14, 17-20) cannot be found in the disclosure as originally filed, which raises the issue of new matter. Applicants argue that support for this limitation can be found in paragraph 0196. Applicant's arguments have been fully considered but they are not persuasive. Paragraph 0196 discloses that it is conceivable and possible that other methionine residues located either upstream or downstream from the amino acid position 1 in the figures may be employed as the starting amino acid residue for the PRO polypeptides. However, the species methionine residue #34 as the starting amino acid is not supported by this generic disclosure because there is no express, implicit, or inherent support for this species to the exclusion of all the other species. In other words, there is no evidence that the disclosure would reasonably lead the skilled artisan to this particular species. This limitation also changes the meaning and scope of the limitation "full-

length coding sequence" (claims 1-6, 12-14, 17-20), which also raises the issue of new matter with respect to the latter.

Support for the limitation "said extracellular domain is amino acids 81-109 or 232-253 of SEQ ID NO: 10" (claims 1-6, 9, 11-13, 17-20) cannot be found in the disclosure as originally, which raises the issue of new matter. Applicants argue that support for this limitation can be found in Figure 10. Applicant's arguments have been fully considered but they are not persuasive. Figure 10 discloses that SEQ ID NO: 10 possesses several transmembrane domains, and thus, the extracellular domains depend on how the polypeptide is arranged in the membrane. Support for the one arrangement implied by the present limitation cannot be found in Figure 10.

Claim Rejections - 35 USC § 102

Claim 14 is rejected under 35 U.S.C. 102(e) as being anticipated by Edwards (U. S. Patent No. 6312922) as evidenced by Stratagene's 1995 catalog (U).

The teachings of Edwards are of record. See the last Office action at page 12, line 18, through page 13, line 27. Edwards also teaches insertion of the cDNA into the BlueScript vector (Example 15, column 21). The BlueScript vector is 2958 bp in length, as evidenced by Stratagene's 1995 catalog (page 334). Edwards Stratagene's BlueScript vector comprising the cDNA is an isolated nucleic acid molecule that is at least about 1000 nucleotides in length and would hybridize to SEQ ID NO: 9, to the coding sequence of SEQ ID NO: 9, and to the coding sequence of the deposited clone, in the absence of evidence to the contrary.

Conclusion

No claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (571) 272-0890. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 7:30 A.M. TO 4:00 P.M. IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, BRENDA BRUMBACK, CAN BE REACHED ON (571) 272-0961.

IF SUBMITTING OFFICIAL CORRESPONDENCE BY FAX, APPLICANTS ARE ENCOURAGED TO SUBMIT OFFICIAL CORRESPONDENCE TO THE CENTRAL FAX NUMBER FOR OFFICIAL CORRESPONDENCE, WHICH IS (571) 273-8300 CUSTOMERS ARE ALSO ADVISED TO USE CERTIFICATE OF FACSIMILE PROCEDURES WHEN SUBMITTING A REPLY TO A NON-FINAL OR FINAL OFFICE ACTION BY FACSIMILE (SEE 37 CFR 1.6 AND 1.8).

FAXED DRAFT OR INFORMAL COMMUNICATIONS SHOULD BE DIRECTED TO THE EXAMINER AT (571) 273-0890.

ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING SHOULD BE DIRECTED TO THE GROUP RECEPTIONIST WHOSE TELEPHONE NUMBER IS (703) 308-0196.

DAVID ROMEO
PRIMARY EXAMINER
ART UNIT 1647

DSR
MARCH 10, 2005